

Butter and Plant-Based Oils Intake and Mortality

Yu Zhang, MBBS; Katia S. Chadaideh, PhD; Yanping Li, PhD; Yuhua Li, SM; Xiao Gu, PhD; Yuxi Liu, PhD; Marta Guasch-Ferré, PhD; Eric B. Rimm, ScD; Frank B. Hu, MD, PhD; Walter C. Willett, MD, DrPH; Meir J. Stampfer, MD, DrPH; Dong D. Wang, MD, ScD

IMPORTANCE The relationship between butter and plant-based oil intakes and mortality remains unclear, with conflicting results from previous studies. Long-term dietary assessments are needed to clarify these associations.

OBJECTIVE To investigate associations of butter and plant-based oil intakes with risk of total and cause-specific mortality among US adults.

DESIGN, SETTING, AND PARTICIPANTS This prospective population-based cohort study used data from 3 large cohorts: the Nurses' Health Study (1990-2023), the Nurses' Health Study II (1991-2023), and the Health Professionals Follow-up Study (1990-2023). Women and men who were free of cancer, cardiovascular disease (CVD), diabetes, or neurodegenerative disease at baseline were included.

EXPOSURES Primary exposures included intakes of butter (butter added at the table and from cooking) and plant-based oil (safflower, soybean, corn, canola, and olive oil). Diet was assessed by validated semiquantitative food frequency questionnaires every 4 years.

MAIN OUTCOMES AND MEASURES Total mortality was the primary outcome, and mortality due to cancer and CVD were secondary outcomes. Deaths were identified through the National Death Index and other sources. A physician classified the cause of death based on death certificates and medical records.

RESULTS During up to 33 years of follow-up among 221 054 adults (mean [SD] age at baseline: 56.1 [7.1] years for Nurses' Health Study, 36.1 [4.7] years for Nurses' Health Study II, and 56.3 [9.3] years for Health Professionals Follow-up Study), 50 932 deaths were documented, with 12 241 due to cancer and 11 240 due to CVD. Participants were categorized into quartiles based on their butter or plant-based oil intake. After adjusting for potential confounders, the highest butter intake was associated with a 15% higher risk of total mortality compared to the lowest intake (hazard ratio [HR], 1.15; 95% CI, 1.08-1.22; *P* for trend < .001). In contrast, the highest intake of total plant-based oils compared to the lowest intake was associated with a 16% lower total mortality (HR, 0.84; 95% CI, 0.79-0.90; *P* for trend < .001). There was a statistically significant association between higher intakes of canola, soybean, and olive oils and lower total mortality, with HRs per 5-g/d increment of 0.85 (95% CI, 0.78-0.92), 0.94 (95% CI, 0.91-0.96), and 0.92 (95% CI, 0.91-0.94), respectively (all *P* for trend < .001). Every 10-g/d increment in plant-based oils intake was associated with an 11% lower risk of cancer mortality (HR, 0.89; 95% CI, 0.85-0.94; *P* for trend < .001) and a 6% lower risk of CVD mortality (HR, 0.94; 95% CI, 0.89-0.99; *P* for trend = .03), whereas a higher intake of butter was associated with higher cancer mortality (HR, 1.12; 95% CI, 1.04-1.20; *P* for trend < .001). Substituting 10-g/d intake of total butter with an equivalent amount of total plant-based oils was associated with an estimated 17% reduction in total mortality (HR, 0.83; 95% CI, 0.79-0.86; *P* < .001) and a 17% reduction in cancer mortality (HR, 0.83; 95% CI, 0.76-0.90; *P* < .001).

CONCLUSIONS AND RELEVANCE In this cohort study, higher intake of butter was associated with increased mortality, while higher plant-based oils intake was associated with lower mortality. Substituting butter with plant-based oils may confer substantial benefits for preventing premature deaths.

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Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Dong D. Wang, MD, ScD, Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, 181 Longwood Ave, Boston, MA 02115 (dow471@mail.harvard.edu).

Over the past few decades, the health effects of dietary fatty acids have been extensively studied.¹⁻⁴ It is well established that substituting saturated fatty acids with unsaturated fatty acids and eliminating trans fatty acids confers substantial health benefits, particularly in the prevention of cardiovascular disease (CVD).^{1,3} However, major food sources of fatty acids contain a mix of fats, and dietary choices are typically based on whole foods rather than individual fatty acids. Butter, rich in saturated fats, and plant-based oils, which are high in unsaturated fats, represent 2 distinct categories with potentially different health impacts.⁵ While butter has been traditionally linked to adverse health outcomes, especially cardiovascular risk,⁶ recent studies have yielded mixed results on butter consumption and mortality.⁷⁻¹¹ A meta-analysis of 15 cohorts concluded that butter has a small or neutral association with CVD, diabetes, and mortality.¹² However, this analysis did not explicitly compare butter with alternative foods, instead implying a comparison to the typical Western diet, which is replete with other unhealthy components like refined grains, sugars, starches, and red meat.¹² In contrast, in clinical trials, plant-based oils like olive, canola, and soybean oils, rich in unsaturated fats, have been linked to improved lipid profiles and reduced inflammation.¹³ Long-term epidemiological studies have also linked plant-based oils to a lower risk of cancer, CVD, and type 2 diabetes.¹⁴⁻¹⁷ However, most evidence focuses on olive oil, and studies on other oils are limited.¹⁸ Furthermore, many studies fail to specify comparison food sources, which is essential for translating findings into actionable dietary recommendations.

We therefore conducted this analysis leveraging dietary information repeatedly collected during decades-long follow-ups in 3 large ongoing cohorts: the Nurses' Health Study (NHS), the Nurses' Health Study II (NHSII), and the Health Professionals Follow-up Study (HPFS). We hypothesized that butter intake was associated with higher all-cause mortality and mortality from CVD and cancer, while plant-based oils were associated with lower mortality. Additionally, we hypothesized that replacing butter with plant-based oils in the diet would confer a substantial reduction in mortality risk.

Methods

Study Population

The NHS began in 1976 and enrolled 121 701 women aged 30 to 55 years. The HPFS started in 1986 and recruited 51 525 men aged 40 to 75 years at baseline. The NHSII was initiated in 1989 and included 116 430 women aged 25 to 42 years at enrollment. All 3 cohorts sent biennial questionnaires to participants to collect information on lifestyle factors and health conditions. The follow-up for mortality was close to complete; the cumulative active follow-up of the cohorts exceeded 90% of potential person-time.^{19,20} The baseline for this analysis was set to 1990 for the NHS and HPFS and 1991 for the NHSII because these were the first cycles in which olive oil intake was assessed using a food frequency questionnaire (FFQ). Participants with a history of CVD, diabetes, or cancer; those without butter and plant-based oil intake data at baseline; and those

Key Points

Question What are the associations of long-term intakes of butter and plant-based oils with mortality in the US population?

Findings In this cohort study of 221 054 adults from 3 large cohorts, higher butter intake was associated with increased total and cancer mortality, while higher intake of plant-based oils was associated with lower total, cancer, and cardiovascular disease mortality.

Meaning Substituting butter with plant-based oils, particularly olive, soybean, and canola oils, may confer substantial benefits for preventing premature deaths.

reporting implausible energy intake (total energy intake <500 or >3500 kcal/d for women and <800 or >4200 kcal/d for men) were excluded from the analysis. A total of 158 463 women and 29 508 men were included in the final analysis.

The study protocol was approved by the institutional review boards of the Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health and those participating registries as required. Completion of the questionnaire was considered to imply informed consent.

Dietary Assessment

Dietary intake was measured using a validated semiquantitative FFQ comprising more than 130 food items, administered at baseline and every 4 years.²¹⁻²³ Participants reported the frequency and quantity of specific foods, types of fats and oils, and the brands or types of oils used for cooking and added at the table over the preceding year. Total butter intake was calculated by multiplying the frequency of consumption by 5 g per pat from the sum of 3 FFQ items: butter from butter and margarine blend, spreadable butter added to food and bread (excluding cooking), and butter used in baking and frying at home. The intake of plant-based oils (corn, safflower, soybean, canola, and olive) was estimated based on the reported oil brand and type of fat used for various cooking methods, including frying, sautéing, baking, and salad dressing, and all of the food composition data for calculating oil intakes were updated every 4 years. The moderate to high validity and reproducibility of butter and olive oil intakes have been reported previously.²⁴ To capture the overall dietary pattern, we calculated the Alternative Healthy Eating Index (AHEI) based on 9 items of foods and nutrients (excluding alcohol and polyunsaturated components), scored as 0 to 90, with higher scores representing healthier diets.²⁵ Alcohol intake was calculated by summing alcohol contents across all alcoholic beverages. Nutrient intakes were calculated by multiplying the consumption of each food by its nutrient content, summing the products across all foods, using values from the Harvard University Food Composition Database.²⁶

Ascertainment of Mortality

Deaths were identified through systematic searches of state vital records and the National Death Index, supplemented by reports from next of kin and postal authorities. Using these

methods, we achieved more than 98% completeness in mortality follow-up for the cohorts.¹⁹ A physician, blinded to data on food consumption and other risk factors, reviewed death certificates, medical records, or autopsy reports to determine the cause of death. The causes were classified according to the *International Classification of Diseases, Eighth Revision (ICD-8)*, for NHS and *Ninth Revision (ICD-9)* for HPFS. CVD deaths were categorized under *ICD-8* codes 390 to 458 and *ICD-9* codes 390 to 459. Cancer-related deaths were identified using *ICD-8* codes 140 to 207 and *ICD-9* codes 140 to 208.

Statistical Analysis

To better represent long-term dietary intake and dampen random measurement errors, we calculated cumulative average intakes of butter and plant-based oil by averaging all previous dietary assessments up to the end of each 4-year follow-up interval. We stopped updating diet after participants reported a diagnosis of diabetes, stroke, or cancer to reduce reverse causation bias. Participants were initially categorized into quartiles of intake levels; however, due to the right-skewed distribution of these exposures, the sample sizes within each category were uneven. Therefore, we labeled the categories as levels 1 to 4 instead of quartiles 1 to 4. We calculated person-time from the return date of the baseline questionnaire to the date of death or the end of follow-up (January 2023), whichever occurred first.

We applied age-stratified Cox proportional hazards regression models to estimate hazard ratios (HRs) and 95% CIs, comparing participants in higher intake categories to those in the lowest category of butter or plant-based oil intake. Linear trends were quantified by modeling the median intake within each category continuously and assessing with the Wald test. Models were adjusted for age, calendar time, total energy intake, mutual adjustments of butter and plant-based oils and non-soybean oil component of mayonnaise, menopausal status and hormone use in women, race and ethnicity, body mass index (BMI), alcohol intake, smoking status, physical activity level, AHEI, aspirin and multivitamin use, baseline histories of hypertension and hypercholesterolemia, and family histories of myocardial infarction, cancer, and diabetes. We also estimated HRs for a 10-g/d increment in butter and plant-based oil intakes by modeling the intake levels as continuous variables. All of the covariates, except for family history of myocardial infarction, cancer, diabetes, and baseline histories of hypertension and hypercholesterolemia, were treated as time varying, with details provided in the footnotes of the tables.

We quantified the associations between the intakes of butter and plant-based oils with mortality in prespecified subgroups defined by physical activity level, age, AHEI, alcohol intake, BMI, baseline hypercholesterolemia, baseline hypertension, smoking status, and sex. We assessed whether the magnitude of associations differed across subgroups by using likelihood ratio tests in a pooled dataset, comparing models with and without the interaction terms.

We quantified estimated effects in the risk of mortality when replacing 10 g/d intake of total butter with an equivalent amount of plant-based oils (total, excluding olive oil, olive oil, or soybean oil) by building substitution models.

The model included simultaneous continuous variables for butter and a specific plant-based oil and was adjusted for the aforementioned covariates. Differences in coefficients were interpreted as the effect of substituting butter with a specific plant-based oil while keeping total energy intake constant.²⁷ We tested for interdependence between butter and plant-based oils by including interaction terms in the model and observed no statistically significant interactions (all *P* for interaction > .05). We also conducted a range of sensitivity analyses to test the robustness of findings (eMethods in Supplement 1).

Unless otherwise specified, analyses were conducted separately within each cohort and pooled using fixed-effect meta-analysis when heterogeneity *P* > .05. All analyses were performed using SAS, version 9.4 (SAS Institute). Two-sided *P* < .05 was considered statistically significant.

Results

Participants Characteristics

During up to 33 years of follow-up among 221 054 US adults (5 427 173 person-years; mean [SD] age at baseline: 56.1 [7.1] years for NHS, 36.1 [4.7] years for NHSII, and 56.3 [9.3] years for HPFS), 50 932 deaths were documented (30 369 in NHS, 4291 in NHSII, and 16 272 in HPFS), with 12 241 due to cancer and 11 240 due to CVD. Participant characteristics are summarized in Table 1. Participants with higher total butter intake had higher BMI and energy intake and were more likely to currently smoke, but they were less likely to be physically active and to use multivitamins. Participants with higher total plant-based oil intake had higher total energy intake and alcohol consumption and were more likely to be physically active.

Total Mortality

The associations between total butter intake and total mortality were consistent in 2 multivariable-adjusted models across all 3 cohorts (Table 2 and eTable 1 in Supplement 1). After adjusting for potential confounders, participants with the highest intake (level 4) of total butter had a 15% higher total mortality compared to those with the lowest intake (level 1) (HR, 1.15; 95% CI, 1.08-1.22; *P* for trend < .001). In contrast, comparing the highest to the lowest intake of total plant-based oil was associated with a 16% lower total mortality (HR, 0.84; 95% CI, 0.79-0.90; *P* for trend < .001). Similarly, across the intake categories, a higher intake of plant oil excluding olive oil was associated with an 8% lower total mortality (comparing extreme levels: HR, 0.92; 95% CI, 0.86-0.98; *P* for trend < .001). In the sensitivity analyses (eTable 2 in Supplement 1), the positive associations of total butter intake with total mortality and the inverse associations between plant-based oil and total mortality remained largely unchanged.

When examining butter for different culinary uses, no statistically significant association was observed between butter used for baking and frying and total mortality. However, each 5-g/d increment of butter added to food or bread intake was associated with a 4% increase in total mortality (HR, 1.04; 95% CI, 1.02-1.05; *P* for trend < .001). To address the

Table 1. Age-Standardized Characteristics According to Levels of Butter and Plant-Based Oil Intake at the Midpoint of Follow-Up^a

Characteristic	Participants, % ^b											
	Total butter ^c				Plant-based oil ^c							
					Total				Without olive oil			
Level 1	Level 2	Level 3	Level 4	Level 1	Level 2	Level 3	Level 4	Level 1	Level 2	Level 3	Level 4	
Nurses' Health Study (all female participants)												
Total No.	53 415	6488	2156	1049	38 599	18 691	4686	1132	37 266	19 628	5150	1064
Median intake, g/d	0.1	4.8	8.8	13.1	3.3	8.9	16.1	27.3	1.8	4.9	8.8	15.0
Age, y	68.0	67.1	67.3	68.2	68.4	67.3	66.6	66.5	67.9	67.8	68.4	68.4
BMI	25.5	25.6	25.5	26.3	25.6	25.4	25.2	25.5	25.3	25.7	26.1	26.4
Total energy intake, kcal/d	1682	1842	1945	2073	1624	1823	1946	2046	1612	1819	1977	2082
Alcohol, g/d	4.9	6.3	7.0	6.3	4.2	6.2	7.7	8.1	4.7	5.4	6.4	6.8
Physical activity, MET-h/wk	17.6	16.7	16.6	14.7	16.5	18.3	20.4	20.1	18.0	16.8	16.0	16.1
Past smoking	46.6	46.2	44.5	43.8	43.8	49.7	53.6	53.3	46.6	46.0	46.9	47.2
Current smoking	7.3	10.2	12.6	16.9	7.8	8.6	6.9	8.9	7.1	8.7	11.0	10.9
Premenopausal	0.6	0.5	0.5	1.0	0.6	0.6	0.5	0.5	0.6	0.6	0.5	1.0
Multivitamin use	68.0	65.6	60.9	58.2	67.1	67.9	67.4	65.6	68.6	66.5	62.7	62.5
Aspirin use	46.3	44.0	43.0	44.8	45.6	46.7	46.3	43.5	45.9	46.0	45.4	47.6
Hypercholesterolemia	37.9	30.8	25.3	27.2	36.6	36.7	36.0	34.0	37.0	35.9	35.8	38.4
Hypertension	27.9	26.2	22.9	27.7	28.0	27.3	25.0	25.3	27.2	27.8	29.3	28.3
Family history												
Myocardial infarction	22.6	21.2	19.9	21.6	22.3	22.5	22.4	20.1	22.2	22.6	22.0	23.0
Diabetes	28.6	27.1	24.5	27.1	28.8	27.8	26.5	27.0	28.5	27.8	28.2	29.3
Cancer	13.9	13.7	14.0	13.3	13.8	14.0	14.1	13.3	13.8	13.9	13.9	13.9
Nurses' Health Study II (all female participants)												
Total No.	77 583	9210	2689	924	58 950	24 924	5292	1240	55 416	27 430	6341	1219
Median intake, g/d	0.2	4.2	7.7	12.8	3.1	8.7	15.8	26.0	1.8	4.7	8.5	13.5
Age, y	48.2	48.2	48.4	48.9	48.1	48.5	48.9	49.3	48.2	48.3	48.5	48.6
BMI	27.1	26.8	27.1	27.9	27.2	26.9	26.5	26.5	26.8	27.4	28.1	29.0
Total energy intake, kcal/d	1775	1989	2149	2294	1709	1975	2109	2254	1694	1953	2161	2317
Alcohol, g/d	3.6	4.8	4.8	4.7	3.0	4.8	6.6	7.9	3.7	3.9	4.1	4.1
Physical activity, MET-h/wk	20.6	20.9	19.3	16.5	19.4	21.8	24.6	28.2	21.5	19.1	18.8	16.8
Past smoking	25.3	29.1	27.3	28.2	23.5	29.1	33.4	35.2	25.7	25.7	26.4	28.8
Current smoking	7.9	9.5	10.9	9.9	7.9	8.6	8.9	8.3	7.5	9.0	10.3	9.8
Premenopausal	63.2	65.3	66.2	65.1	63.1	64.1	65.9	66.3	63.7	63.4	63.2	60.8
Multivitamin use	93.0	94.0	93.6	89.1	92.2	94.5	96.2	96.2	93.4	93.2	90.7	88.8
Aspirin use	9.3	10.6	10.4	10.2	9.1	10.0	10.3	9.5	9.3	9.6	9.7	8.9
Hypercholesterolemia	14.6	12.0	13.5	14.1	14.6	13.8	13.8	12.6	14.2	14.4	14.8	16.6
Hypertension	6.1	5.5	4.8	7.3	6.3	5.8	5.1	4.7	5.8	6.2	7.5	8.3
Family history												
Myocardial infarction	42.5	40.6	40.2	42.0	42.2	42.1	43.2	44.0	42.4	41.9	42.5	41.3
Diabetes	39.0	37.6	35.4	37.3	39.0	38.1	38.4	36.6	38.5	39.0	38.6	41.9
Cancer	52.2	54.3	55.9	50.6	51.6	53.8	55.7	57.2	52.8	52.4	50.8	49.1
Health Professionals Follow-up Study (all male participants)												
Total No.	22 312	2935	1101	531	14 143	8887	3071	778	14 230	8639	3148	862
Median intake, g/d	0.1	4.1	8.1	14.0	3.0	7.4	12.7	21.4	1.8	4.6	8.0	12.9
Age, y	67.6	66.8	67.4	69.4	67.9	67.0	67.4	67.3	67.5	67.2	67.9	69.0
BMI	26.1	26.3	26.2	26.6	26.2	26.1	26.1	26.6	26.0	26.3	26.4	26.5
Total energy intake, kcal/d	1953	2146	2301	2555	1859	2096	2267	2426	1852	2091	2300	2452
Alcohol, g/d	12.3	14.5	14.9	14.5	10.7	13.7	17.1	19.9	12.3	13.1	13.5	12
Physical activity, MET-h/wk	28.2	28.3	27.6	28.2	27.0	28.8	30.8	32.8	28.3	28.0	28.5	27.6
Past smoking	52.7	51.8	52.6	46.7	50.8	53.5	55.3	60.6	52.4	52.6	53.5	49.5
Current smoking	4.0	5.9	5.6	8.4	4.2	4.5	4.8	4.9	3.9	4.6	5.4	7.7

(continued)

Table 1. Age-Standardized Characteristics According to Levels of Butter and Plant-Based Oil Intake at the Midpoint of Follow-Up^a (continued)

Characteristic	Participants, % ^b				Plant-based oil ^c							
	Total butter ^c				Total				Without olive oil			
	Level 1	Level 2	Level 3	Level 4	Level 1	Level 2	Level 3	Level 4	Level 1	Level 2	Level 3	Level 4
Multivitamin use	60.1	57.3	55.8	52.6	59.3	59.2	60.5	59.6	60.8	59.0	55.0	54.9
Aspirin use	76.2	74.5	72.9	68.3	74.8	77.0	76.1	74.7	75.3	76.5	75.9	72.9
Hypercholesterolemia	29.7	20.5	18.9	12.8	28.0	28.0	27.0	27.4	28.8	27.8	25.0	24.1
Hypertension	22.3	18.9	18.1	17.4	22.3	21.1	20.5	19.8	21.8	21.8	20.6	21.0
Family history												
Myocardial infarction	32.2	28.6	27.9	26.1	31.3	31.9	30.8	31.5	31.7	31.7	29.6	32.4
Diabetes	22.9	21.6	20.4	16.3	22.6	22.4	22.9	23.0	22.5	22.6	22.4	24.7
Cancer	38.2	38.3	39.3	36.8	38.0	38.1	39.6	37.2	37.6	38.6	39.1	41.3

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); MET-h/wk, metabolic equivalent hours per week.

^a Data are presented at the midpoint of follow-up: 2002 for the Nurses' Health Study and the Health Professionals Follow-up Study, and 2003 for the Nurses' Health Study II. Intake levels 1 to 4 represent the lowest to highest intake categories, respectively, based on intake distributions over the follow-up.

Due to the highly right-skewed nature of these intake variables, the sample sizes within each category are unevenly distributed.

^b Unless otherwise indicated, data are presented as means. All variables except age were age standardized.

^c Level 1 indicates the lowest intake and level 4 the highest intake.

Table 2. Associations of Intakes of Total Butter and Plant-Based Oil With Total Mortality Risk^a

	Levels of intake ^b				P for trend	Total mortality ^c
Variable	Level 1	Level 2	Level 3	Level 4		
Total butter						
Median intake (NHS/NHSII/HPFS), g/d	0.1/0.2/0.1	4.8/4.2/4.1	8.8/7.7/7.1	13.1/12.8/14.0	NA	NA
Total No. of cases	42 766	5242	1780	1144	NA	NA
Model 1, HR (95% CI) ^d	1 [Reference]	1.08 (1.05-1.11)	1.08 (1.03-1.13)	1.41 (1.33-1.50)	<.001	1.21 (1.17-1.25)
Model 2, HR (95% CI) ^e	1 [Reference]	1.03 (1.00-1.06)	1.00 (0.95-1.05)	1.15 (1.08-1.22)	<.001	1.07 (1.03-1.10)
Total plant-based oil						
Median intake (NHS/NHSII/HPFS), g/d	3.3/3.1/3.0	8.9/8.7/7.4	16.1/15.8/12.7	27.3/26.0/21.4	NA	NA
Total No. of cases	31 601	14 513	3811	1007	NA	NA
Model 1, HR (95% CI) ^d	1 [Reference]	0.83 (0.81-0.85)	0.73 (0.71-0.76)	0.74 (0.69-0.79)	<.001	0.79 (0.78-0.81)
Model 2, HR (95% CI) ^e	1 [Reference]	0.89 (0.87-0.91)	0.83 (0.80-0.86)	0.84 (0.79-0.90)	<.001	0.87 (0.85-0.89)
Total plant-based oil without olive oil						
Median intake (NHS/NHSII/HPFS), g/d	1.8/1.8/1.8	4.9/4.7/4.6	8.8/8.5/8.0	15.0/13.5/12.9	NA	NA
Total No. of cases	28 963	15 720	4980	1269	NA	NA
Model 1, HR (95% CI) ^d	1 [Reference]	0.94 (0.92-0.97)	0.87 (0.84-0.91)	0.93 (0.87-0.99)	<.001	0.88 (0.84-0.92)
Model 2, HR (95% CI) ^e	1 [Reference]	0.94 (0.92-0.96)	0.88 (0.85-0.92)	0.92 (0.86-0.98)	<.001	0.88 (0.84-0.93)

Abbreviations: HPFS, Health Professionals Follow-up Study; HR, hazard ratio; NA, not applicable; NHS, Nurses' Health Study; NHSII, Nurses' Health Study II.

^a All results are pooled from the 3 cohorts using the fixed-effect meta-analysis model.

^b Level 1 indicates the lowest intake and level 4 the highest intake.

^c The HRs of total mortality were calculated per 10-g/d increase in total butter, total plant-based oil, or total plant-based oil without olive oil intake.

^d Model 1 was adjusted for age (months), calendar time (years), total energy intake (kcal/d, in quintiles), butter and plant-based oils (g/d, by intake levels; mutually adjusted), and non-soybean oil component of mayonnaise intake (g/d, in quartiles).

^e Model 2 was adjusted for age (months), calendar time (years), total energy intake (kcal/d, in quintiles), non-soybean oil component of mayonnaise intake (g/d, in quartiles), menopausal status and hormone use in women

(premenopausal, postmenopausal never users, postmenopausal past users, or postmenopausal current users), White race (yes vs no), body mass index (calculated as weight in kilograms divided by height in meters squared; <21, 21-24.9, 25-29.9, 30-31.9, or ≥32), alcohol consumption (0, 0.1-4.9, 5.0-9.9, 10.0-14.9, 15.0-29.9, or ≥30 g/d), smoking status (never, past, current with 1-14 cigarettes/d, current with 15-24 cigarettes/d, or current with ≥25 cigarettes/d), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, or ≥27.0 metabolic equivalent hours per week), Alternative Healthy Eating Index (without the alcohol and polyunsaturated components; scored as 0-90, with higher scores representing healthier diets; in quintiles), aspirin and multivitamin use (yes vs no), baseline histories of hypertension and hypercholesterolemia (yes vs no), and family history of myocardial infarction, cancer, and diabetes (yes vs no). Intakes of butter and plant-based oils (g/d, by intake levels) were mutually adjusted.

possibility that the observed association for butter added to bread might reflect residual confounding due to incomplete adjustment for refined grain intake, 2 sensitivity analyses were conducted adjusting for white bread intake and glycemic load, both of which yielded results consistent with the main

results (eTable 3 in Supplement 1). In contrast, there was a statistically significant association between higher intakes of specific types of plant-based oils, including canola oil, soybean oil, and olive oil, and lower total mortality, with HRs per 5-g/d increment of 0.85 (95% CI, 0.78-0.92), 0.94

(95% CI, 0.91-0.96), and 0.92 (95% CI, 0.91-0.94), respectively (all *P* for trend < .001). Meanwhile, no statistically significant associations with total mortality were observed for corn and safflower oils (Table 3 and eTable 4 in Supple-

ment 1). The associations of butter and plant-based oil intakes with total mortality were generally consistent across subgroups defined by age, BMI, and lifestyle factors (Table 4).

Table 3. Association of Intakes of Different Butter or Oil Types With Total Mortality Risk^a

Variable	Levels of intake ^b				P for trend	Total mortality ^c
	Level 1	Level 2	Level 3	Level 4		
Butter from baking and frying						
Median intake (NHS/NHSII/HPFS), g/d	0.0/0.0/0.0	1.9/1.8/2.1	3.6/3.4/3.9	6.7/5.8/7.2	NA	NA
Total No. of cases	48 218	1818	639	257	NA	NA
Model 1, HR (95% CI) ^d	1 [Reference]	0.98 (0.93-1.02)	1.05 (0.97-1.13)	1.13 (1.00-1.28)	.19	1.04 (0.98-1.11)
Model 2, HR (95% CI) ^e	1 [Reference]	0.98 (0.93-1.02)	1.01 (0.94-1.10)	1.04 (0.92-1.18)	.91	1.00 (0.94-1.07)
Butter added to food or bread						
Median intake (NHS/NHSII/HPFS), g/d	0.0/0.1/0.0	2.6/2.5/2.1	5.0/5.0/4.5	12.5/10.8/11.0	NA	NA
Total No. of cases	39 716	9615	2864	2037	NA	NA
Model 1, HR (95% CI) ^d	1 [Reference]	1.06 (1.03-1.09)	1.10 (1.06-1.15)	1.23 (1.18-1.29)	<.001	1.10 (1.08-1.12)
Model 2, HR (95% CI) ^e	1 [Reference]	1.03 (1.00-1.05)	1.03 (0.99-1.07)	1.09 (1.04-1.14)	<.001	1.04 (1.02-1.05)
Corn oil						
Median intake (NHS/NHSII/HPFS), g/d	0.0/0.0/0.0	1.3/1.3/1.8	2.7/2.3/3.5	4.9/4.1/6.7	NA	NA
Total No. of cases	47 847	1980	827	278	NA	NA
Model 1, HR (95% CI) ^d	1 [Reference]	1.03 (0.98-1.09)	1.11 (1.03-1.20)	1.15 (1.01-1.30)	.001	1.14 (1.06-1.23)
Model 2, HR (95% CI) ^e	1 [Reference]	1.01 (0.96-1.06)	1.09 (1.01-1.17)	1.05 (0.92-1.19)	.09	1.07 (0.99-1.15)
Safflower oil						
Median intake (NHS/NHSII/HPFS), g/d	0.0/0.0/0.0	1.0/0.8/1.2	1.9/1.4/2.2	3.9/3.2/4.6	NA	NA
Total No. of cases	50 396	322	148	66	NA	NA
Model 1, HR (95% CI) ^d	1 [Reference]	0.90 (0.80-1.00)	0.98 (0.83-1.15)	0.91 (0.72-1.16)	.11	0.84 (0.67-1.04)
Model 2, HR (95% CI) ^e	1 [Reference]	0.94 (0.84-1.04)	1.03 (0.87-1.21)	0.91 (0.72-1.16)	.33	0.90 (0.72-1.11)
Canola oil						
Median intake (NHS/NHSII/HPFS), g/d	0.0/0.0/0.0	1.5/1.3/1.7	3.0/2.6/3.2	5.4/4.8/5.9	NA	NA
Total No. of cases	47 839	2201	653	239	NA	NA
Model 1, HR (95% CI) ^d	1 [Reference]	0.89 (0.85-0.94)	0.89 (0.82-0.97)	0.86 (0.75-1.00)	<.001	0.80 (0.74-0.87)
Model 2, HR (95% CI) ^e	1 [Reference]	0.93 (0.89-0.98)	0.90 (0.82-0.98)	0.90 (0.78-1.04)	<.001	0.85 (0.78-0.92)
Soybean oil						
Median intake (NHS/NHSII/HPFS), g/d	1.6/1.5/1.4	4.6/4.5/4.1	8.6/8.2/7.0	14.1/13.0/11.4	NA	NA
Total No. of cases	31 116	14 329	4271	1216	NA	NA
Model 1, HR (95% CI) ^d	1 [Reference]	0.95 (0.92-0.98)	0.89 (0.84-0.93)	0.94 (0.87-1.01)	<.001	0.95 (0.92-0.97)
Model 2, HR (95% CI) ^e	1 [Reference]	0.93 (0.90-0.96)	0.89 (0.84-0.93)	0.91 (0.84-0.98)	<.001	0.94 (0.91-0.96)
Olive oil						
Median intake (NHS/NHSII/HPFS), g/d	0.5/0.6/0.5	7.3/7.3/5.9	14.1/14.1/10.3	23.6/23.0/18.5	NA	NA
Total No. of cases	43 295	5480	1571	574	NA	NA
Model 1, HR (95% CI) ^d	1 [Reference]	0.81 (0.79-0.84)	0.71 (0.67-0.75)	0.73 (0.67-0.80)	<.001	0.88 (0.87-0.89)
Model 2, HR (95% CI) ^e	1 [Reference]	0.89 (0.86-0.91)	0.80 (0.76-0.84)	0.82 (0.76-0.89)	<.001	0.92 (0.91-0.94)

Abbreviations: HPFS, Health Professionals Follow-up Study; HR, hazard ratio; NA, not applicable; NHS, Nurses' Health Study; NHSII, Nurses' Health Study II.

^a All values are pooled from the 3 cohorts using the fixed-effects meta-analysis model.

^b Level 1 indicates the lowest intake and level 4 the highest intake.

^c The HRs of total mortality were calculated per 5-g/d increase in total butter from baking and frying; butter from butter, margarine blend, and spreadable butter; or individual sources of plant-based oil.

^d Model 1 was adjusted for age (months), calendar time (years), total energy intake (kcal/d, in quintiles), butter and plant-based oils (g/d, by intake levels; mutually adjusted), and non-soybean oil component of mayonnaise intake (g/d, in quartiles).

^e Model 2 was adjusted for age (months), calendar time (years), total energy intake (kcal/d, in quintiles), non-soybean oil component of mayonnaise intake (g/d, in quartiles), menopausal status and hormone use in women

(premenopausal, postmenopausal never users, postmenopausal past users, or postmenopausal current users), White race (yes vs no), body mass index (calculated as weight in kilograms divided by height in meters squared; <21, 21-24.9, 25-29.9, 30-31.9, or ≥32), alcohol consumption (0, 0.1-4.9, 5.0-9.9, 10.0-14.9, 15.0-29.9, or ≥30 g/d), smoking status (never, past, current with 1-14 cigarettes/d, current with 15-24 cigarettes/d, or current with ≥25 cigarettes/d), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, or ≥27.0 metabolic equivalent hours per week), Alternative Healthy Eating Index (without the alcohol and polyunsaturated components; scored as 0-90, with higher scores representing healthier diets; in quintiles), aspirin and multivitamin use (yes vs no), baseline histories of hypertension and hypercholesterolemia (yes vs no), and family history of myocardial infarction, cancer, and diabetes (yes vs no). Intakes of butter and plant-based oils (g/d, by intake levels) were mutually adjusted.

Table 4. Associations of Intake of Total Butter and Plant-Based Oil With Risk of Total Mortality in Subgroups^{a,b}

	Levels of intake, HR (95% CI) ^c				P for trend	Total mortality, HR (95% CI) ^d	P for interaction ^e
Variable	Level 1	Level 2	Level 3	Level 4			
Total butter							
Physical activity							
<Median	1 [Reference]	1.03 (1.00-1.06)	1.01 (0.96-1.06)	1.15 (1.09-1.23)	<.001	1.07 (1.04-1.11)	.26
≥Median	1 [Reference]	1.18 (0.79-1.76)	0.57 (0.21-1.54)	2.62 (1.22-5.64)	.18	1.40 (0.86-2.29)	
Age, y							
<50	1 [Reference]	1.01 (0.94-1.10)	0.99 (0.86-1.14)	1.20 (0.99-1.44)	.23	1.08 (0.98-1.19)	.10
≥50	1 [Reference]	1.03 (1.00-1.07)	0.98 (0.93-1.04)	1.15 (1.07-1.24)	.002	1.06 (1.01-1.12)	
AHEI							
Low	1 [Reference]	1.04 (1.00-1.08)	0.99 (0.93-1.06)	1.19 (1.11-1.27)	<.001	1.07 (1.03-1.12)	.87
High	1 [Reference]	1.01 (0.96-1.07)	1.01 (0.91-1.12)	1.12 (0.95-1.32)	.34	0.99 (0.92-1.07)	
Alcohol intake							
Moderate	1 [Reference]	1.07 (0.99-1.16)	1.01 (0.89-1.15)	1.07 (0.90-1.27)	.26	1.05 (0.97-1.15)	.34
Nonmoderate	1 [Reference]	1.01 (0.98-1.05)	0.96 (0.91-1.02)	1.17 (1.09-1.25)	.01	1.03 (0.99-1.07)	
BMI							
<30	1 [Reference]	1.03 (0.99-1.07)	1.01 (0.96-1.07)	1.19 (1.11-1.27)	<.001	1.06 (1.03-1.10)	.24
≥30	1 [Reference]	1.03 (0.95-1.12)	0.92 (0.80-1.06)	1.08 (0.92-1.27)	.80	0.99 (0.91-1.08)	
Hypertension							
No	1 [Reference]	1.02 (0.98-1.06)	0.94 (0.88-1.00)	1.13 (1.05-1.22)	.13	1.02 (0.98-1.07)	.43
Yes	1 [Reference]	1.05 (0.99-1.11)	1.12 (1.01-1.23)	1.20 (1.07-1.34)	<.001	1.10 (1.03-1.16)	
Hypercholesterolemia							
No	1 [Reference]	1.03 (0.99-1.07)	1.01 (0.95-1.07)	1.16 (1.08-1.25)	<.001	1.06 (1.02-1.11)	.23
Yes	1 [Reference]	1.03 (0.97-1.10)	0.93 (0.83-1.04)	1.09 (0.96-1.25)	.61	0.99 (0.93-1.06)	
Smoking status							
Never/past	1 [Reference]	1.03 (0.99-1.06)	0.99 (0.94-1.05)	1.16 (1.08-1.25)	.001	1.05 (1.01-1.09)	.90
Current	1 [Reference]	1.02 (0.93-1.12)	0.99 (0.84-1.15)	1.09 (0.93-1.27)	.001	1.02 (0.93-1.11)	
Sex							
Female	1 [Reference]	1.04 (1.00-1.07)	0.97 (0.91-1.03)	1.15 (1.07-1.24)	.005	1.06 (1.02-1.11)	.23
Male	1 [Reference]	1.00 (0.95-1.05)	1.03 (0.95-1.12)	1.09 (0.99-1.21)	.12	1.05 (0.99-1.11)	
Total plant-based oil							
Physical activity							
<Median	1 [Reference]	0.88 (0.86-0.90)	0.83 (0.80-0.86)	0.84 (0.78-0.89)	<.001	0.87 (0.85-0.89)	.32
≥Median	1 [Reference]	0.96 (0.72-1.29)	1.02 (0.64-1.60)	0.69 (0.29-1.62)	.65	0.94 (0.72-1.23)	
Age, y							
<50	1 [Reference]	0.82 (0.77-0.87)	0.82 (0.74-0.92)	0.69 (0.56-0.85)	<.001	0.80 (0.75-0.85)	.13
≥50	1 [Reference]	0.89 (0.87-0.92)	0.82 (0.78-0.86)	0.85 (0.78-0.86)	<.001	0.87 (0.84-0.90)	
AHEI							
Low	1 [Reference]	0.88 (0.85-0.91)	0.81 (0.76-0.86)	0.81 (0.72-0.90)	<.001	0.82 (0.79-0.85)	.23
High	1 [Reference]	0.88 (0.85-0.92)	0.82 (0.78-0.87)	0.83 (0.75-0.92)	<.001	0.88 (0.85-0.91)	
Alcohol intake							
Moderate	1 [Reference]	0.88 (0.83-0.94)	0.77 (0.69-0.85)	0.91 (0.77-1.06)	<.001	0.89 (0.83-0.94)	.05
Nonmoderate	1 [Reference]	0.88 (0.86-0.90)	0.82 (0.78-0.86)	0.77 (0.71-0.84)	<.001	0.83 (0.81-0.85)	
BMI							
<30	1 [Reference]	0.89 (0.86-0.91)	0.83 (0.79-0.86)	0.84 (0.78-0.92)	<.001	0.85 (0.83-0.88)	.69
≥30	1 [Reference]	0.86 (0.81-0.92)	0.79 (0.71-0.89)	0.71 (0.58-0.86)	<.001	0.82 (0.78-0.88)	
Hypertension							
No	1 [Reference]	0.87 (0.84-0.89)	0.79 (0.75-0.83)	0.80 (0.73-0.87)	<.001	0.83 (0.81-0.86)	.85
Yes	1 [Reference]	0.91 (0.87-0.95)	0.88 (0.82-0.95)	0.89 (0.77-1.02)	<.001	0.88 (0.85-0.92)	
Hypercholesterolemia							
No	1 [Reference]	0.88 (0.86-0.91)	0.81 (0.77-0.86)	0.82 (0.75-0.90)	<.001	0.85 (0.83-0.88)	.96
Yes	1 [Reference]	0.88 (0.85-0.92)	0.83 (0.78-0.89)	0.84 (0.74-0.96)	<.001	0.85 (0.81-0.88)	
Smoking status							
Never/past	1 [Reference]	0.89 (0.87-0.92)	0.82 (0.79-0.86)	0.87 (0.80-0.94)	<.001	0.87 (0.85-0.89)	.01
Current	1 [Reference]	0.90 (0.83-0.98)	0.91 (0.79-1.04)	0.67 (0.52-0.87)	.41	0.84 (0.77-0.90)	
Sex							
Female	1 [Reference]	0.87 (0.85-0.89)	0.80 (0.76-0.84)	0.77 (0.71-0.85)	<.001	0.85 (0.83-0.88)	.83
Male	1 [Reference]	0.91 (0.88-0.95)	0.87 (0.82-0.92)	0.92 (0.84-1.02)	<.001	0.91 (0.87-0.95)	

(continued)

Table 4. Associations of Intake of Total Butter and Plant-Based Oil With Risk of Total Mortality in Subgroups^{a,b} (continued)

	Levels of intake, HR (95% CI) ^c				P for trend	Total mortality, HR (95% CI) ^d	P for interaction ^e
Variable	Level 1	Level 2	Level 3	Level 4			
Plant-based oil without olive oil							
Physical activity							
<Median	1 [Reference]	0.94 (0.92-0.96)	0.89 (0.85-0.92)	0.92 (0.86-0.99)	<.001	0.88 (0.84-0.93)	.25
≥Median	1 [Reference]	0.78 (0.55-1.11)	0.77 (0.42-1.41)	0.93 (0.43-1.99)	.59	0.85 (0.48-1.52)	
Age, y							
<50	1 [Reference]	0.88 (0.82-0.94)	0.78 (0.69-0.88)	0.72 (0.58-0.88)	<.001	0.74 (0.65-0.85)	.18
≥50	1 [Reference]	0.94 (0.91-0.97)	0.89 (0.84-0.93)	0.91 (0.84-0.98)	<.001	0.88 (0.83-0.93)	
AHEI							
Low	1 [Reference]	0.91 (0.88-0.94)	0.86 (0.81-0.91)	0.84 (0.77-0.92)	<.001	0.84 (0.79-0.89)	<.001
High	1 [Reference]	0.97 (0.93-1.01)	0.91 (0.84-0.98)	0.99 (0.88-1.12)	.14	1.00 (0.93-1.07)	
Alcohol intake							
Moderate	1 [Reference]	0.90 (0.83-0.96)	0.85 (0.75-0.96)	0.98 (0.82-1.19)	.06	0.94 (0.83-1.07)	.06
Nonmoderate	1 [Reference]	0.94 (0.91-0.96)	0.88 (0.83-0.92)	0.87 (0.80-0.94)	<.001	0.88 (0.84-0.93)	
BMI							
<30	1 [Reference]	0.93 (0.90-0.95)	0.88 (0.84-0.92)	0.89 (0.82-0.96)	<.001	0.90 (0.85-0.94)	.95
≥30	1 [Reference]	0.93 (0.87-1.00)	0.87 (0.77-0.97)	0.92 (0.77-1.09)	.06	0.85 (0.76-0.95)	
Hypertension							
No	1 [Reference]	0.92 (0.89-0.95)	0.85 (0.80-0.90)	0.83 (0.76-0.91)	<.001	0.86 (0.81-0.91)	.52
Yes	1 [Reference]	0.95 (0.91-1.00)	0.91 (0.84-0.98)	1.00 (0.88-1.13)	.13	0.95 (0.88-1.03)	
Hypercholesterolemia							
No	1 [Reference]	0.91 (0.88-0.94)	0.85 (0.81-0.90)	0.84 (0.76-0.92)	<.001	0.86 (0.81-0.91)	.28
Yes	1 [Reference]	0.97 (0.93-1.02)	0.91 (0.84-0.99)	0.98 (0.87-1.11)	.15	0.95 (0.88-1.03)	
Smoking status							
Never/past	1 [Reference]	0.93 (0.90-0.96)	0.88 (0.84-0.92)	0.89 (0.82-0.96)	<.001	0.89 (0.85-0.94)	.23
Current	1 [Reference]	0.91 (0.83-0.99)	0.79 (0.69-0.91)	0.86 (0.69-1.07)	.01	0.89 (0.78-1.02)	
Sex							
Female	1 [Reference]	0.93 (0.91-0.96)	0.87 (0.83-0.92)	0.90 (0.83-0.99)	<.001	0.87 (0.82-0.92)	.88
Male	1 [Reference]	0.95 (0.91-0.99)	0.91 (0.85-0.97)	0.95 (0.85-1.05)	.02	0.91 (0.84-0.99)	

Abbreviations: AHEI, Alternative Healthy Eating Index; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HR, hazard ratio.

^a All values were pooled from the 3 cohorts (Nurses' Health Study, Nurses' Health Study II, and Health Professionals Follow-up Study) using the fixed-effects meta-analysis model.

^b Multivariable adjusted model adjusted for age (months), calendar time (years), total energy intake (kcal/d, in quintiles), non-soybean oil component of mayonnaise intake (g/d, in quartiles), menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, or postmenopausal current users), White race (yes vs no), BMI (<21, 21-24.9, 25-29.9, 30-31.9, or ≥32), alcohol consumption (0, 0.1-4.9, 5.0-9.9, 10.0-14.9, 15.0-29.9, or ≥30 g/d), smoking status (never, past, current with 1-14 cigarettes/d, current with 15-24 cigarettes/d, or current with ≥25

cigarettes/d), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, or ≥27.0 metabolic equivalent hours per week), AHEI (without the alcohol and polyunsaturated components; scored as 0-90, with higher scores representing healthier diets; in quintiles), aspirin and multivitamin use (yes vs no), baseline histories of hypertension and hypercholesterolemia (yes vs no), and family history of myocardial infarction, cancer, and diabetes (yes vs no), except the variable of stratification. Intakes of butter and plant-based oils (g/d, by intake levels) were mutually adjusted.

^c Level 1 indicates the lowest intake and level 4 the highest intake.

^d The HRs of total mortality were calculated per 10-g/d increase in total butter, total plant-based oil, or plant-based oil without olive oil.

^e P for interaction was obtained using likelihood ratio tests comparing models with and without the interaction terms in a pooled dataset.

Cause-Specific Mortality

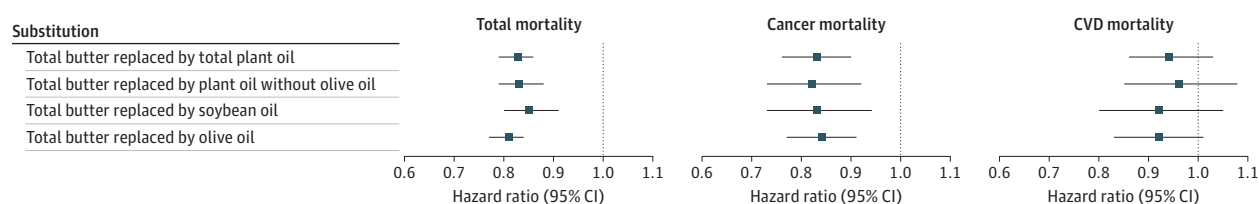
For cause-specific mortality (eTables 5 and 6 in [Supplement 1](#)), every 10-g/d increment in total plant-based oil intake was associated with an 11% lower risk of cancer mortality (HR, 0.89; 95% CI, 0.85-0.94; P for trend < .001) and a 6% lower risk of CVD mortality (HR, 0.94; 95% CI, 0.89-0.99; P for trend = .03). Higher butter intake was associated with an increased risk of cancer mortality (per 10 g/d: HR, 1.12; 95% CI, 1.04-1.20; P for trend < .001), but no statistically significant association was found with CVD mortality. Olive oil intake was inversely associated with both cancer mortality (per 5 g/d: HR, 0.96; 95% CI, 0.93-0.98; P for trend = .001) and CVD mortality (per 5 g/d: HR, 0.97; 95% CI, 0.94-1.00; P for trend = .04). Additionally, higher intakes of canola oil and soybean oil were both associated with a lower risk of cancer

mortality, with HRs per 5-g/d increment of 0.81 (95% CI, 0.69-0.96) and 0.94 (95% CI, 0.89-0.99), respectively.

Substitution Analysis

Replacing 10 g/d of total butter intake by an equivalent amount of total plant-based oil was associated with an estimated 17% reduction in total mortality (HR, 0.83; 95% CI, 0.79-0.86; P < .001), a 17% reduction in cancer mortality (HR, 0.83; 95% CI, 0.76-0.90; P < .001), and a 6% reduction in CVD mortality, although the latter was not statistically significant (HR, 0.94; 95% CI, 0.86-1.03; P = .17) ([Figure](#)). Similarly, the HRs of total mortality when substituting 10 g/d of total butter with plant oils excluding olive oil, soybean oil, and olive oil were 0.83 (95% CI, 0.79-0.88), 0.85 (95% CI, 0.80-0.91), and 0.81 (95% CI, 0.77-0.84), respectively. The corresponding HRs for

Figure. Estimated Effects of Substituting Butter With Different Plant-Based Oils on Mortality Risk



Hazard ratios with 95% CIs (error bars) of total mortality, cancer mortality, and cardiovascular disease (CVD) mortality in association with a 10-g/d substitution of total butter with (1) total plant-based oil, (2) plant-based oil minus olive oil, (3) soybean oil, and (4) olive oil. This multivariable-adjusted model was adjusted for age (months), calendar time (years), total energy intake (kcal/d, in quintiles), non-soybean oil component of mayonnaise intake (g/d, in quartiles), menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, or postmenopausal current users), White race (yes vs no), body mass index (calculated as weight in kilograms divided by height in meters squared; <21, 21-24.9, 25-29.9, 30-31.9, or ≥ 32), alcohol consumption (0, 0.1-4.9, 5.0-9.9, 10.0-14.9, 15.0-29.9, or ≥ 30 g/d), smoking status (never, past,

current with 1-14 cigarettes/d, current with 15-24 cigarettes/d, or current with ≥ 25 cigarettes/d), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, or ≥ 27.0 metabolic equivalent hours per week), Alternative Healthy Eating Index (without the alcohol and polyunsaturated components; scored as 0-90, with higher scores representing healthier diets; in quintiles), aspirin and multivitamin use (yes vs no), baseline histories of hypertension and hypercholesterolemia (yes vs no), and family history of myocardial infarction, cancer, and diabetes (yes vs no). Intakes of butter and plant-based oils (g/d, by intake levels) were mutually adjusted. All values were pooled from the 3 cohorts (Nurses' Health Study, Nurses' Health Study II, and Health Professionals Follow-up Study) using the fixed-effect meta-analysis model.

cancer mortality were 0.82 (95% CI, 0.73-0.92) for plant oils excluding olive oil, 0.83 (95% CI, 0.73-0.94) for soybean oil, and 0.84 (95% CI, 0.77-0.91) for olive oil. Substituting butter with specific plant-based oils was associated with a lower risk of CVD mortality, but the findings were not statistically significant.

Discussion

In 3 large prospective cohorts of US women and men, we found that higher butter intake was associated with increased total and cancer mortality. In contrast, higher intakes of plant-based oils were associated with lower risk of total mortality and mortality due to cancer and CVD. The inverse associations were consistent for specific types of plant-based oils, including olive oil, soybean oil, and canola oil, but not for corn and safflower oils. In the substitution analysis, replacing butter with an equivalent amount of total plant-based oils in the diet was associated with estimated reductions in total and cancer mortality risk.

Previous studies examining the associations between butter intake and total mortality have been limited and yielded inconsistent results, with some reporting positive associations and others finding no statistically significant associations.^{7,12,28,29} For instance, the Netherlands Cohort Study found an 8% (95% CI, 1%-15%) higher risk of death among women who ate butter compared to those who did not.⁷ However, the dichotomization of butter intake in this study prevented a thorough examination of the relationship across the intake range. Another study conducted in Sweden found that higher butter intake was associated with higher diastolic blood pressure but did not report a statistically significant association with CVD.²⁸ In contrast to these previous findings, the present study identified a positive association between butter intake and both total and cancer mortality, which aligned with prior research demonstrating the adverse health effects of dairy fats. For instance, a study from the Netherlands indicated that

high-fat dairy product intake was associated with an increased risk of CVD mortality.³⁰ Additionally, the cohorts assessed in this study have also shown that higher intakes of total dairy fat and whole milk were associated with an increased risk of total mortality.³¹

Notably, in sensitivity analyses using only baseline dietary data, we observed a weakening association between butter and plant-oil intake with mortality compared to results from cumulative dietary data. Most previous studies, which only assessed diet at baseline, are prone to measurement errors when estimating long-term intake. For instance, a study using data from the National Institutes of Health-AARP Diet and Health Study found similar associations to the present study with weaker associations, likely due to the use of only baseline dietary data.³² This difference in the assessment of dietary data increased the robustness of the present findings, as our use of cumulative data better reflects sustained dietary habits over time.

We found that butter intake was associated with cancer mortality. Previous studies have shown that high dairy intake was associated with prostate, ovarian, and colorectal cancer.^{31,33,34} Another study of the cohorts assessed in this study included butter as part of the dairy intake in the analysis and found that higher high-fat dairy foods were associated with a higher risk of developing hepatocellular carcinoma and breast cancer.^{35,36} The high saturated fat content in butter can trigger adipose tissue inflammation, a key pathogenic pathway in the development of various cancers. Moreover, studies have shown that dietary saturated fats can alter hormonal activity, influencing hormone-sensitive cancers such as breast and prostate cancer.³⁷⁻³⁹ The differential associations between different uses of butter and mortality warrant further investigation. It is plausible that the lack of a statistically significant association with mortality for butter used in baking and frying might be attributed to the relatively small quantities and less frequent use of butter for this culinary purpose, resulting in small between-person variation and limiting our ability to isolate its health effects. Additionally, dur-

ing cooking, some butter may remain in the pan or be present in dishes in ways that are not easily identifiable by participants, unlike butter used as a spread, potentially increasing the degree of nondifferential misclassification in its measurement and leading to attenuated associations. Notably, the 2 sensitivity analyses in this study, which further adjusted for white bread intake and glycemic load, yielded results consistent with the primary findings. These findings suggest that the observed differential associations are unlikely attributable to residual confounding from incomplete adjustment for refined grain intake.

Inverse associations between olive oil intake and CVD and mortality have been well documented in large cohort studies and clinical trials.^{16,40–42} However, there is a relative scarcity of large prospective cohort studies investigating the association of other plant-based oils, which are major sources of polyunsaturated fatty acids, with mortality. The present findings indicate that intake of plant-based oils excluding olive oil is still inversely associated with mortality risk, with the strongest associations observed for soybean oil and canola oil. These results align with our previous analyses, which demonstrated that higher linoleic acid intake, primarily derived from vegetable oils, is associated with lower total mortality risk.^{2,43} Previous randomized clinical trials have shown that incorporating soybean oil into the diet, especially as a substitute for butter, can lower circulating cholesterol levels and reduce the risk of coronary heart disease and total mortality.^{44,45} These oils are rich in polyunsaturated fats, which are known to confer considerable benefits for heart health, including decreasing low-density lipoprotein cholesterol, reducing inflammation, and lowering mortality risk.^{16,40,41} Additionally, their higher antioxidant content, particularly vitamin E, may protect against oxidative stress and related chronic diseases.^{46,47} Although the association for corn oil did not reach statistical significance, a borderline positive trend was observed. This should be interpreted with caution due to low average consumption. It is possible that high-temperature commercial frying can oxidize unsaturated fats and produce harmful by-products, potentially diminishing its health benefits.⁴⁸ Moreover, corn oil was one of the plant-based oils more likely to be partially hydrogenated and to contain trans fats in earlier follow-up periods.⁴⁹ However, a prior study we conducted analyzed corn oil under various home-frying conditions and found no meaningful changes in its fatty acid composition. It is also possible that corn oil alone does not share the full benefit of soybean or canola oil because it contains minimal amounts of omega-3 fatty acids. Furthermore, we observed associations that were not statistically significant between total plant-based oils and CVD mortality in men. This may be due to differences in consumption patterns across the cohorts, as participants in HPFS consumed higher amounts of corn oil and lower amounts of soybean and olive oils than participants in NHSI and NHSII. However, no statistically significant interactions were found between sex and plant oil intakes. Meanwhile, the data on safflower oil are limited and difficult to interpret due to the wide confidence intervals, which could be attributed to its lower consumption among the population. It is also important to note that the estimated intakes of plant

oils (excluding olive oil) in the cohorts included in this study were lower than those in the general population, likely due to these oils being reported separately rather than included as distinct items on the FFQ, as was the case for olive oil. However, this underreporting is largely nondifferential and, therefore, unlikely to systematically bias the observed associations with mortality.

Importantly, prior research has consistently highlighted the need to specify comparison foods when assessing health effects. However, most of the previous studies failed to explicitly identify a comparison food.^{2,50} We address these limitations in this study by conducting substitution analyses, which revealed that replacing butter with plant-based oils could lead to a statistically significant reduction in mortality risk. This is consistent with findings from feeding trials, where vegetable oils rich in monounsaturated fatty acids, such as olive oil and high oleic-acid canola oil, consistently demonstrated beneficial effects on lipid profiles and inflammation.^{13,51,52} The present findings are closely aligned with the dietary recommendations of the American Heart Association and the Dietary Guidelines for Americans,⁵³ which advocate for reducing saturated fat intake and replacing it with polyunsaturated and monounsaturated fats to lower the risk of chronic disease.⁴⁴ The present results indicate that replacing 3 small pats of butter (approximately 15 g) with 1 tablespoon of plant-based oil (approximately 15 g) in the daily diet could contribute to lowering the risk of premature mortality.

Strengths and Limitations

The strengths of this study include large sample size, long follow-up duration, and repeated measurements of dietary exposures and covariates. However, the study also has several limitations. First, dietary data from FFQs and other methods are affected by measurement errors, which tend to underestimate association. However, we used cumulative averages to reduce short-term variability and better capture long-term dietary habits. Second, reverse causation may occur, as individuals could alter their diets after developing chronic diseases. To address this, we excluded participants with major chronic diseases at baseline and stopped updating dietary data after diagnoses of diabetes, stroke, or cancer. We also conducted sensitivity analyses using an 8-year lag and baseline diet only, which produced consistent results. Third, it is possible that participants may have mistakenly reported margarine intake as butter intake due to their similar appearance. Additionally, despite adjustment for many confounding variables, residual confounding may still exist. Lastly, the participants in the cohorts included in this study were predominantly White and health care professionals, which may limit the generalizability of the findings but also help minimize potential socioeconomic confounding.

Conclusions

In this cohort study, we found that higher intake of butter was associated with elevated total and cancer mortality, while higher plant-based oils intake was associated with lower total mortal-

ity and mortality due to cancer and CVD. Substituting butter with plant-based oils may confer substantial benefits for preventing premature deaths. These results support current dietary recommendations to replace animal fats like butter with nonhy-

drogenated vegetable oils that are high in unsaturated fats, especially olive, soy, and canola oil. Further studies are warranted to uncover the molecular mechanisms underlying the distinct metabolic effects of butter and plant-based oils.

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Author Affiliations: Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts (Zhang, Yuhan Li, Liu, Rimm, Hu, Willett, Stampfer); Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts (Zhang, Chadaideh, Liu, Rimm, Hu, Willett, Stampfer, Wang); Massachusetts Veterans Epidemiology Research and Information Center, VA Boston Healthcare System, Boston (Yanping Li); Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, Massachusetts (Yanping Li, Gu, Guasch-Ferré, Rimm, Hu, Willett, Stampfer, Wang); Section of Epidemiology, Department of Public Health, University of Copenhagen, Copenhagen, Denmark (Guasch-Ferré); Broad Institute of MIT and Harvard, Cambridge, Massachusetts (Chadaideh, Liu, Wang).

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Concept and design: Zhang, Chadaideh, Hu, Willett, Stampfer, Wang.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Zhang, Wang.

Critical review of the manuscript for important intellectual content: Chadaideh, Yanping Li, Yuhan Li, Gu, Liu, Guasch-Ferré, Rimm, Hu, Willett, Stampfer, Wang.

Statistical analysis: Zhang, Chadaideh, Yanping Li, Yuhan Li, Gu, Liu, Willett.

Obtained funding: Wang.

Administrative, technical, or material support:

Chadaideh, Hu, Willett, Stampfer, Wang.

Supervision: Rimm, Wang.

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